Contains Nonbinding Recommendations

Draft Guidance on Buprenorphine Hydrochloride; Naloxone Hydrochloride

This draft guidance, once finalized, will represent the Food and Drug Administration's (FDA's) current thinking on this topic. It does not create or confer any rights for or on any person and does not operate to bind FDA or the public. You can use an alternative approach if the approach satisfies the requirements of the applicable statutes and regulations. If you want to discuss an alternative approach, contact the Office of Generic Drugs.

Active ingredient: Buprenorphine Hydrochloride; Naloxone Hydrochloride

Form/Route: Sublingual Tablet/Oral

Recommended study: 1 study

Type of study: Fasting
Design: Single-dose, two-treatment, two-period crossover in-vivo
Strength: 8 mg/2mg (base)
Subjects: Healthy males and nonpregnant females, general population
Additional Comments:
A naltrexone blockade should be used to remove the risk of any opioid-related adverse events. Naltrexone should be administered well in advance of dosing to achieve adequate blockade of opioid receptors. The most common approach is to administer 50 mg of naltrexone at the following times: (1) 12 hours prior to dosing; (2) at the time of study drug dosing; and (3) 12 hours after the last dose of study drug. Please consult with a physician who is an expert in the administration of opioids for an appropriate dose of narcotic antagonist.

Analytes to measure (in appropriate biological fluid): Buprenorphine and its active metabolite, norbuprenorphine, and Naloxone (total and unconjugated), in plasma.

Please submit the metabolite data as supportive evidence of comparable therapeutic outcome. For the metabolite, the following data should be submitted: individual and mean concentrations, individual and mean pharmacokinetic parameters, and geometric means and ratios of means for AUC and Cmax.

Bioequivalence based on (90% CI): Buprenorphine and Naloxone

Waiver request of in-vivo testing: 2 mg/0.5 mg (base) strength based on (i) acceptable bioequivalence study on the 8 mg/2 mg (base) strength, (ii) acceptable in-vitro dissolution testing of all strengths, and (iii) proportional similarity of the formulations across all strengths.

Dissolution test method and sampling times:

Please note that a **Dissolution Methods Database** is available to the public at the OGD website at http://www.accessdata.fda.gov/scripts/cder/dissolution/. Please find the dissolution information for this product at this website. Please conduct comparative dissolution testing on 12 dosage units each of all strengths of the test and reference products. Specifications will be determined upon review of the application